UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,878	11/21/2005	Hiroshi Takahashi	0760-0346PUS1	9660

2292 7590 02/04/2009
BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
02/04/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/533,878	TAKAHASHI ET AL.	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,7 and 10-17* is/are pending in the application.

4a) Of the above claim(s) *11,12,15 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,7,10,13,14 and 17* is/are rejected.

7)☒ Claim(s) *1,13 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed November 12, 2008 in response to the Office Action of May 14, 2008, is acknowledged and has been entered. Claims 1-3, 6, 7, 10-17 are currently pending. Claim 17 is new. Claims 4, 5, 8, and 9 are canceled. Previously pending claims 1 and 6 have been amended. Claims 11, 12, 15, and 16 remain withdrawn. Claims 1-3, 6, 7, 10, 13, 14, and 17 are currently being examined as drawn to the elected species of "examining nucleic acids" and "HTLV-1 gene".

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Examiner suggests a title relevant to examining ATL cells expressing SF-25 antigen.

Claim Objections

3. Claim 1 is objected to because of the following informalities: Claim 1 in the conclusion recites: "examining said **collected cancer cells which are bound to said magnetic beads**, wherein **cell binding to the magnetic beads is indicative of cancer cell** that expresses SF-25 antigen". This phrase is grammatically inconsistent with plural and singular references to the cells. Examiner suggests amended the reference to "cell" to be plural in order to remain grammatically consistent in the claims, i.e. "wherein cells binding to the magnetic beads are indicative of cancer cells that express SF-25 antigen." Appropriate correction is required.

4. Claims 13 and 17 are objected to because of the following informalities: Claim 13 recites "HTLV-1" and claim 17, which is dependent on claim 13, recites "HTLV-1 proviral gene," however, no proviral gene is recited in claim 13. Examiner recognizes these are the same nucleic acid, however, to remain consistent in terminology the claims should recite the same name when referring to the same nucleic acid for clear antecedent basis.

New Rejections

(necessitated by amendments)

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 6 is dependent on claim 5 which is canceled, hence, the metes and bounds of the claims cannot be determined. For examination purposes, Examiner will assume claim 6 is dependent on claim 1.

6. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 17 provides for the use of examination of HTLV-1 proviral gene in a method of diagnosing smoldering ATL cells, but, since the claim does not set forth any steps involved in the method/process, it is unclear what

method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-3, 6, 7, 10, 13, 14 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (J Cancer Res Clin Oncol, 2001, 127:489-494) in view of WO 93/06117 (Wands et al, published April 1993, IDS), Suzuki et al (Blood, 1999, vol. 94, p. 98a, supplement1, part 1; abstract #430, IDS), and Takemoto et al (Blood, 1994, 84:3080-3085).

The claims are drawn to a method for examining a sample containing cancer cells comprising contacting a sample comprising at least one type of smoldering adult T cell leukemia cells separated from a body, with magnetic beads utilizing antigen-antibody reaction between said cancer cells and an anti-SF-25 antibody or antigen-binding fragment thereof, then collecting said magnetic beads by magnetic force to collect cells bound to said magnetic beads, and examining said collected cancer cells

which are bound to said magnetic beads, wherein cell binding to the magnetic beads is indicative of a cancer that expresses SF-25 antigen (claims 1 and 2), wherein said cancer cells are those contained in blood (claims 3 and 10), wherein said cancer cells are smoldering adult T cell leukemia cells (ATL cells) (claim 6), wherein the examination is of nucleic acids (claim 7), wherein said examination of nucleic acid include examination of HTLV-1 (claim 13), wherein said examination includes PCR (claim 14), the method of claim 13, wherein examination of HTLV-1 proviral gene is utilized in a method for diagnosing smoldering ATL cells (claim 17).

Park et al teach immunomagnetic beads coated with an antibody specific for a cancer antigen expressed by cancer cells and using said immunomagnetic beads for the separation and isolation of said cancer cells that express the antigen and examining the isolated cancer cells using RT-PCR (abstract, p. 490, col. 1 and 2). The cancer cells were separated from a human body and contained in blood (abstract; p. 490, col. 2). Park et al teach that immunomagnetic bead selection successfully isolates and concentrates cancer cells expressing the antigen recognized by the antibody comprised by the bead, provides a more sensitive method for RT-PCR analysis than regular RT-PCR, and decreases chances of false positives in RT-PCR analysis (p. 493, col. 1). The immunobead RT-PCR assay relies on a preliminary isolation of tumor cells from body fluids, which is then followed by amplification of one or more mRNA markers by RT-PCR (p. 493, col. 1). Park et al teach that the feasibility and the prognostic value of immunobead RT-PCR assay, which combines the enrichment of cancer cells by immunomagnetic bead selection and the RT-PCR amplification of tumor-specific

mRNAs, has been demonstrated in several studies of breast, prostate, and gastrointestinal cancers (p. 492, col. 2).

Park et al does not teach that the immunomagnetic beads utilize SF-25 antibody, examining smoldering ATL cells, or examining the HTLV-1 gene.

Wands et al teach that the SF-25 antigen has been shown by immunohistochemical staining to be expressed by several human tumor types including leukemia (p. 6, line 29 through p. 7, line 8; p. 15, lines 1-12). Wands et al teach preparation of the SF-25 monoclonal antibody (p. 11, lines 23 through p. 12, line 13; p. 19-23) and using the SF-25 antibody to bind and detect tissue or SF-25 antigen in a sample including blood samples (p. 12, lines 14-22; p. 40-41). Wands et al teach that for immunodiagnostic assays, SF-25 antibody can be attached to various labels and to solid supports including magnetite, and the support material can be in the form of beads (p. 41, lines 6 to p. 42, line 2).

Suzuki et al teach that adult T-cell leukemia (ATL) cells highly express SF-25 antigen (abstract).

Takemoto et al teach examining peripheral blood mononuclear cell and lymph node cell samples of ATL patients including smoldering ATL patients, by using inverse PCR (IPCR) to detect HTLV-1 proviral DNA (abstract; p. 3080, col. 1 through p. 3081, col. 1). Takemoto et al teach that ATL comprises different clinical states or stages including smoldering ATL (p. 3080, col. 1). Takemoto et al teach that determining clonality of HTLV-1 proviral DNA is essential to diagnosis of ATL (abstract; p. 3080, col. 1; p. 3083, both columns), wherein all ATL types including smoldering ATL were

identified by detection of monoclonality in integrated HTLV-1 provirus (p. 3083, col. 2; Table 1). IPCR is a rapid and powerful tool for analysis of the clinical states of ATL and can identify a small number of ATL cells in a sample (p. 3080, col. 2). With IPCR, "it is now possible to more precisely diagnose smoldering ATL" (p. 3084, col. 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use immunomagnetic beads with SF-25 antibodies to isolate and examine a sample comprising smoldering ATL cells using the immunomagnetic bead enrichment and nucleic acid examination method taught by Park et al because Wands et al and Suzuki et al teach that leukemic or ATL cells express SF-25 antigen and smoldering ATL is a stage of ATL as taught by Takemoto et al, and Wands et al teach that the SF-25 antibodies can be used in conjunction with magnetite and beads for immunodiagnostic assays. One would have been motivated to use immunomagentic SF-25 antibody isolation for examining ATL cells including smoldering ATL cells in order to enrich the sample cell population with leukemia cells for diagnostic examination and because Wands suggests the SF-25 can be attached to magnetite and beads for diagnostic examination of cancer cells expressing SF-25 antigen. One of ordinary skill in the art would have a reasonable expectation of success using the immunomagnetic beads with SF-25 antibodies to isolate and enrich a sample comprising smoldering ATL cells given that smoldering ATL cells are a stage of ATL and ATL cells are known to highly express SF-25.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to examine the HTLV-1 gene by PCR in the sample

comprising smoldering ATL cells isolated by immunomagnetic beads in order to diagnose ATL, including smoldering ATL as taught by Takemoto et al, and because Park et al teach that immunomagnetic bead-enriched cancer cells and be examined by PCR. One would have been motivated to examine the sample that is enriched in order to more precisely and efficiently diagnose smoldering ATL so the patient can receive proper treatment, and because enriched cell populations yield higher sensitivity and specificity for nucleic acid examination. One would have a reasonable expectation of success in examining an enriched sample comprising smoldering ATL cells for HTVL-1 by PCR because Park et al demonstrate increased sensitivity and specificity for nucleic acid detection from cancer cells enriched by immunomagnetic bead selection and Takemoto et al demonstrate successful PCR examination of HTLV-1 nucleic acid in leukemic cells for diagnosis of smoldering ATL.

Response to Relevant Arguments

8. Applicants argue that none of the references disclose or teach that SF-25 can be a marker of smoldering ATL and that Applicants were the first to discover that a substantial percentage of mononuclear cells from smoldering ATL patients express SF-25 antigen so that smoldering ATL can be diagnosed by utilizing the expression of FS-25 as an index. Applicants reiterate that none of the cited references disclose that mononuclear cells of smoldering ATL express SF-25 antigen (p. 5-6).

The arguments have been considered but are not found persuasive. As taught by Suzuki et al it is known in the art that ATL cells express SF-25 antigen. Given

smoldering ATL cells are ATL cells, it is reasonably expected that they express SF-25 and are successfully isolated by the method of the combined references.

9. Examiner notes that all ATL cells of all stages tested in the specification express SF-25 antigen (Table 1), therefore SF-25 expression is not unique to smoldering ATL cells and would not distinguish them from other ATL cells. Takemoto et al, however, teach that determining clonality of HTLV-1 proviral DNA in ATL precisely diagnoses smoldering ATL.

10. All other rejections recited in the Office Action mailed May 14, 2008 are hereby withdrawn.

11. **Conclusion:** No claim is allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. ' 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY

PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Primary Examiner, Art Unit 1642